

**IN THE UNITED STATES PATENT AND TRADEMARK
OFFICE**

In re Application of: David E. Weinstein Docket No.: 5402-9

Serial No.: 10/035,914 Examiner: Diana B. Johannsen

Filed: November 7, 2001 Group Art Unit: 1634

Title: **METHODS FOR INHIBITING
PROLIFERATION OF ASTROCYTES AND
ASTROCYTIC TUMOR CELLS AND USES
THEREOF**

August 9, 2004

Commissioner for Patents P.O. Box 1450
Alexandria, VA 22313-1450

**CORRECTED AMENDMENT IN RESPONSE TO JANUARY 29,
2004 [NON-FINAL] OFFICE ACTION
AND REQUEST FOR THREE (3) MONTH EXTENSION OF TIME**

Sir:

Applicant respectfully responds to the Office Action dated January 29,
2004 as follows:



AMENDMENT TO THE TITLE

Please delete the title and replace it with the following:

METHODS FOR DETECTING ASTROCYTOMAS AND MONITORING THE TREATMENT THEREOF

AMENDMENT TO THE CLAIMS

33. (currently amended) A method for assessing the efficacy of astrocytoma therapy in a subject who has undergone or is undergoing treatment for an astrocytoma, the method comprising assaying for CD81 expression a diagnostic sample ~~of cells~~ of astrocytic tumor cells of the subject, wherein no detection of expression of CD81 in astrocytic tumor cells of the subject is indicative of unsuccessful astrocytoma therapy.

34. (currently amended) The method of claim 33, wherein the diagnostic sample ~~of cells~~ of astrocytic tumor cells ~~lineage~~ of the subject is assayed *in vitro*.

A complete listing of all claims (1-64) in the application pursuant to 37 C.F.R. § 1.121 is attached hereto.

REMARKS

Claims 31-64 are pending in this application. By this amendment, applicant has amended the title of the application to be descriptive of the subject matter now claimed, and has amended claims 33 and 34 solely to



clarify the wording of the claims. After amendment, claims 31-64 are currently pending. No new matter is added by the foregoing amendments. Thus, entry of the foregoing amendments, and reconsideration of this application in view of the current amendments and the remarks which follow, are respectfully requested.

Objection to the Title

The Examiner objected to the title of the application and required a new title. Applicant has amended the title of the application so that it is now descriptive of the subject matter claimed. Applicant submits that the title "METHODS FOR DETECTING ASTROCYTOMAS AND MONITORING THE TREATMENT THEREOF" is clearly indicative of the invention to which claims 31-64 are directed. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Rejection of Claims 31-64 Under 35 USC § 112, First Paragraph

The Examiner has rejected claims 31-64 under 35 USC § 112(1) based upon lack of enablement. Specifically, the Examiner has stated that the specification does not provide data showing an association between astrocytomas and the absence of CD81 expression in astrocytic tumor cells from a subject. In the Examiner's view, it cannot be predicted whether the lack of CD81 expression observed by applicant in cultured cells also occurs in primary tumor cells; therefore, the data showing lack of expression of CD81 in astrocytic cell lines are insufficient. Applicant respectfully traverses the rejection.



Applicant believes that the specification does provide evidence showing an association between astrocytic tumors and the absence of CD81 expression *in vivo*. Applicant refers to paragraphs 137-138 of the instant specification, which provide evidence that withdrawal of astrocytes from the cell cycle is CD81-dependent. As paragraphs 137-138 show, astrocytes from CD81-/- animals showed a doubling of astrocyte proliferation. It is well accepted in the art that loss of growth control is a characteristic of tumorigenic cells. Paragraph 140 of the instant specification emphasizes the link between tumorigenesis and loss of growth control in the following statement: "Tumorigenesis is a multistep phenomenon which contributes to a loss of growth control."

Moreover, the specification (at paragraph 32) states that a "subject" may be any animal. The CD81-/- animals discussed at paragraphs 137-138 are clearly "subjects" falling within the scope of claims 31-64. Accordingly, applicant asserts that the disclosures in the instant specification showing a doubling of astrocyte proliferation in astrocytes from CD81-/- animals, combined with both the knowledge in the art and the portions of the specification cited by the Examiner, are sufficient to enable the subject matter of claims 31-64.

In connection with claim 33 and the claims dependent therefrom, the Examiner has stated that undue experimentation is required to practice the claimed methods, because there is no "evidence that any type of astrocytoma therapy administered to a subject ...alters CD81 expression in astrocytic tumor cells of the subject."

With respect, applicant notes that claim 33 and its dependent claims are directed to a method for assessing the efficacy of astrocytoma



therapy by assaying for CD81 expression. In order for these claims to satisfy the enablement requirement of 35 USC § 112(1), applicant's specification does not need to set forth a method for determining whether CD81 expression is altered by astrocytoma therapy; this is not the subject of the claim. Rather, to enable claim 33 and its dependent claim, applicant's specification must provide support for the claimed method of assaying for CD81 expression.

Applicant submits that techniques for carrying out the claimed assay for CD81 expression are described in great detail in the instant specification. *See, e.g.*, paragraphs 81-96. Accordingly, applicant asserts that the disclosures in the instant specification are also sufficient to enable the subject matter of claim 33 and its dependent claims.

Based upon the foregoing, applicant respectfully requests reconsideration and withdrawal of the rejection.

Rejection of Claims 31-64 Under 35 USC § 112, Second Paragraph

The Examiner has rejected claims 31, 32, and 35-51 under 35 USC § 112(2) based upon indefiniteness. Specifically, the Examiner has stated that recitation of the language "diagnostic sample of cells of astrocytic lineage" is unclear and has requested clarification. Applicant respectfully traverses the rejection.

As used throughout the specification and claims, the phrase "diagnostic sample" refers to any sample that may be used in a diagnostic assay or test. The term "diagnostic" is not meant to limit the word "sample," it merely provides a *context* in which the sample is employed. Specifically, in the instant application, a diagnostic sample is repeatedly used in the context of

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diagnosing (i.e., determining the cause or nature of a disease or condition).

For example, in paragraph 17 of the instant specification, a diagnostic sample is assayed for CD81 expression in order to determine whether a subject has an astrocytoma. In this context, the diagnostic sample is used to diagnose an astrocytoma by determining astrocytoma to be the cause of the subject's condition. Similarly, in paragraph 18 of the specification, a diagnostic sample is assayed for CD81 expression in order to assess the efficacy of astrocytoma therapy in a subject undergoing such treatment. In this context, the diagnostic sample is used to determine the nature of an astrocytoma that has already been identified, which is just another form of diagnosis.

Based upon the specification, then, the "diagnostic sample" that is recited in claims 31, 32, and 35-51 is simply a sample that is used in the context of a diagnosis. Accordingly, applicant respectfully submits that the term "diagnostic sample," as it appears in claims 31, 32 and 35-51, is not indefinite. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

The Examiner has also rejected claims 32, 48, and 51 under 35 USC § 112(2) based upon indefiniteness. Specifically, the Examiner has stated that recitation of the language "wherein the diagnostic sample of cells of astrocytic lineage of the subject is assayed *in vitro*" is indefinite, as it does not make clear whether the assay for CD81 expression should, itself, be performed *in vitro*, or whether an additional, subsequent *in vitro* assay should be performed after the assaying step of claim 31.

Applicant respectfully traverses the rejection. According to the



specification, at paragraph 83, "the diagnostic sample of cells of astrocytic lineage of the subject may be assayed for CD81 expression *in vitro*, or *in vivo* in a subject." Consistent with this portion of the specification, independent claims 31 and 33 encompass *in vitro* and *in vivo* methods for assaying CD81 expression - both of which are disclosed in the subject application. Dependent claims 32, 48 and 51 are limited to the *in vitro* type of assay. Therefore, the term "*in vitro*," as used in claims 32, 48, 51, is further limiting of the assaying step in claims 31 and 33, such that the previously recited "assaying for CD81 expression" in claim 31 or 33 is, itself, to be performed *in vitro*. Based upon the foregoing, applicant respectfully submits that the term "*in vitro*," as it appears in claims 32, 48 and 51, is not indefinite. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Additionally, the Examiner has rejected claims 33-34 and 52-64 under 35 USC § 112(2), based upon indefiniteness. Specifically, the Examiner has stated that recitation of the language "diagnostic sample of cells of astrocytic tumor cells" is unclear, and has requested clarification. Applicant has amended claims 33 and 34 to remove the repetitive language "of cells." With respect to use of the word "diagnostic" in claims 33-34 and 52-64, applicant refers above to his comments in response to the rejection of claims 31, 32 and 35-51 under 35 USC § 112(2).

Claims 33 and 34, as amended, now recite "diagnostic sample of astrocytic tumor cells," which applicant submits is not indefinite in view of the specification and the comments set forth above; claims 52-64, which depend from amended claims 33 and 34, are not indefinite for the same reasons. Accordingly, reconsideration and withdrawal of the rejection is



respectfully requested.

Finally, the Examiner has rejected claims 34, 61, and 64 under 35 USC § 112(2), based upon indefiniteness. Specifically, the Examiner has stated that recitation of the language "wherein the diagnostic sample of cells of astrocytic lineage of the subject is assayed *in vitro*" is unclear, and that there is no antecedent basis for the phrase "diagnostic sample of cells of astrocytic lineage."

Applicant has amended claim 34 to provide an antecedent basis for the language "diagnostic sample of cells of astrocytic lineage." With respect to use of the word "*in vitro*" in claims 34, 61 and 64, applicant refers above to his comments in response to the rejection of claims 32, 48 and 51 under 35 USC § 112(2).

Claim 34, as amended, now recites "the diagnostic sample of astrocytic tumor cells of the subject is assayed *in vitro*," which applicant submits is not indefinite in view of the specification and the comments set forth above; claims 61 and 64, which depend from amended claim 34, are not indefinite for the same reasons.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.



CONCLUSION

Applicant believes that he has fully responded to the Examiner's concerns, and that each of the claims is in condition for immediate allowance. Applicant respectfully requests reconsideration and allowance of all pending claims.

Authorization is also hereby provided to charge any fees, or credit any overpayments, that may be required to Deposit Account 503033.

By: /Sander Rabin/

Sander Rabin MD JD
Reg. No. 53,496
Customer No. 41672
Attorney for Applicants
Convergent Technology Patent Law Group™
WHITEMAN OSTERMAN & HANNA LLC
One Commerce Plaza
Albany, New York 12260
518 487-7683

